Claims

1. A combination of antibodies comprising
   (a) an anti-HPV-16 E7 antibody obtainable by
      (i) eliciting an in vivo humoral response against HPV-16 E7 protein or a fragment thereof in a goat; and
      (ii) affinity-purifying antibodies as obtained in the eliciting-step (i); and
   (b) an anti-HPV-18 E7 antibody.

2. The combination of antibodies of claim 1, wherein said HPV-16 E7 protein or a fragment thereof is recombinantly produced.

3. The combination of antibodies of claim 1 or 2, wherein said HPV-16 E7 protein or said fragment thereof is expressed in E. coli.

4. The combination of antibodies of any one of claims 1 to 3, wherein said HPV-16 E7 protein or said fragment thereof is highly purified.

5. The combination of antibodies of claim 4, wherein said highly purified HPV-16 E7 protein or a fragment thereof is purified by a combination of ion exchange chromatography and gel filtration.

6. The combination of antibodies of claim 5, wherein said purification further comprises, prior to ion exchange chromatography and gel filtration, a protein precipitation step.

7. The combination of antibodies of any one of claims 1 to 6, wherein said affinity purification of the obtained antibodies is carried out over immobilized HPV-16 E7 protein or a fragment thereof.

8. The combination of antibodies of claim 7, wherein said HPV-16 E7 protein or a fragment thereof is immobilized on PVDF membranes, nitrocellulose, sepharose, agarose, DEAE-cellulose or DEAE.

9. The combination of antibodies of any one of claims 1 to 8, wherein said anti-HPV-18 E7 antibody is a polyclonal or monoclonal antibody.

10. The combination of antibodies of claim 9, wherein said anti-HPV-18 E7 polyclonal antibody is derived from a non-human animal selected from the group consisting of rat, mouse, guinea pig, chicken, duck, sheep, horse, goat, pig, cattle and donkey.

11. The combination of antibodies of claim 9, wherein said anti-HPV-18 E7 polyclonal antibody is obtainable by
    (i) eliciting an in vivo humoral response against highly purified HPV-16 E7 protein or a fragment thereof in a rabbit; and
    (ii) affinity-purifying antibodies as obtained in the eliciting-step (i).

12. Use of the combination of antibodies of any one of claims 1 to 11 for the preparation of a diagnostic composition for the (immuno-) histological detection of high risk HPV E7 protein.

13. The use of claim 12, wherein said high risk HPV is HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59.

14. The use of claim 12 or 13, wherein said (immuno-) histological detection is carried out on Pap-smears, cervical (carcinoma) biopsies, anogenital biopsies, mamma biopsies, head- or neck biopsies or prostate biopsies.

15. The use of any one claims 12 to 14, wherein said diagnostic composition is used for evaluating the risk of acquiring a sexually transmitted disease or cancer, for measuring the status of an existing sexually transmitted disease

or cancer, or for screening therapy efficiency in the treatment of a sexually transmitted disease or cancer.

16. A method for the preparation of a diagnostic composition comprising the step of formulating the combination of antibodies of any one of claims 1 to 11 with a diagnostically acceptable carrier, diluent, buffer, or storage solution.

17. The use of any one of claims 12 to 15 or the method of claim 16, wherein said diagnostic composition further comprises suitable means for detection.

18. A diagnostic composition comprising the combination of antibodies of any one of claims 1 to 11 or obtained by the method of claim 16 or 17.

19. A kit comprising the combination of antibodies of any one of claims 1 to 11, or a diagnostic composition of claim 18.

20. An in vitro method for the detection of high risk HPV E7 protein comprising the steps of

a) incubating a biological sample with the combination of antibodies of any one of claims 1 to 11; and

b) measuring and/or detecting E7 protein of high risk HPV,

whereby the presence, the absence or the amount of specifically-bound antibodies of the combination of antibodies of any one of claims 1 to 11 is indicative for the presence of high risk HPV E7 protein.

21. The method of claim 20, wherein said high risk HPV is HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59.

22. The method of claim 20, wherein the detection of high risk HPV E7 protein is used for determining the occurrence of a sexually transmittable disease or cancer.

23. The method of claim 20 further comprising a further step (c), whereby in said step (c) the presence, the absence or the amount of specifically-bound antibodies of the combination of antibodies of any one of claims 1 to 11 of step (b) is compared to the presence, the absence or the amount of specifically-bound antibodies of the combination of antibodies of any one of claims 1 to 11 in a negative or a positive control sample.

24. Use of the combination of antibodies of any one of claims 1 to 11, a diagnostic composition of claim 18 or a kit of claim 19 in an in vitro method for the detection of high risk HPV E7 protein.

25. The method of claim 22 or the use of claim 15 wherein said sexually transmitted disease is a high risk HPV infection or wherein said cancer is cervical cancer, breast cancer/mamma cancer, prostate cancer, head and neck cancer, penile cancer and/or anogenital cancer/neoplasia (AIN).

26. A method for the production of a combination of an anti-HPV-16 E7 antibody and an anti-HPV-18 E7 antibody comprising the steps of
    (a) eliciting an in vivo humoral response against HPV-16 E7 protein or a fragment thereof in a goat;
    (b) affinity-purifying antibodies as obtained in the eliciting-step (a) and
    (c) mixing the antibody of step (b) with an anti-HPV-18 E7 antibody.

27. A method for the production of a combination of an anti-HPV-16 E7 antibody and an anti-HPV-18 E7 antibody comprising the steps of
    (a) eliciting an in vivo humoral response against HPV-16 E7 protein or a fragment thereof and against HPV-18 E7 protein or a fragment thereof in a goat; and
    (b) affinity-purifying antibodies as obtained in the eliciting-step (a).

28. The method of claim 25 or 26, wherein said HPV-16 E7 protein or fragment thereof is highly-purified.

29. The combination of antibodies of any one of claims 1 to 11 or the method of any one of claims 26 to 28, wherein said highly purified HPV-16 E7 protein or said fragment thereof is a native, highly purified HPV-16 E7 protein or a fragment thereof.

30. A diagnostic composition comprising the antibody obtainable as described in step (a) of claim 1 or as obtained by the method of any one of claims 26 to 28.

31. A method for the preparation of a diagnostic composition comprising the step of formulating the antibody of claim 30 with a diagnostically acceptable carrier, diluent, buffer, or storage solution.

32. Use of the antibody obtainable as described in step (a) of claim 1 for the preparation of a diagnostic composition for detecting E7 protein of HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59.

33. Use of the antibody obtainable as described in step (a) of claim 1 for detecting E7 protein of HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59.

34. Use of an antibody combination as obtained by the method of any one of claims 26 to 28 for the preparation of a diagnostic composition for detecting E7 protein of HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59.

35. Use of an antibody combination as obtained by the method of any one of claims 26 to 28 for the preparation of a diagnostic composition for detecting E7 protein of HPV-16 and HPV-18 and HPV-31, HPV-35, HPV-39, HPV-45 and/or HPV-59.

36. Use of an antibody combination as obtained by the method of any one of

claims 26 to 28 for the preparation of a diagnostic composition for detecting E7 protein of HPV-16, HPV-18 and HPV-31.

37. A kit comprising the antibody obtainable as described in step (a) of claim 1 or a diagnostic composition of claim 30.

38. An in vitro method for the detection of HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59 E7 protein comprising the steps of

a) incubating a biological sample with the antibody obtainable as described in step (a) of claim 1 or the antibody combination of any one of claims 1 to 11 or an antibody combination as obtained by the method of any one of claims 26 to 28; and

c) measuring and/or detecting E7 protein of HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-52, HPV-56, HPV-58 and/or HPV-59,

whereby the presence, the absence or the amount of specifically-bound said antibodies is indicative for the presence of high risk HPV E7 protein .